Profile of Mild Behavioral Impairment and Factor Structure of the Mild Behavioral Impairment Checklist in Cognitively Normal Older Adults

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Abstract

Objectives: In this large population study we set out to examine the profile of Mild Behavioral Impairment using the Mild Behavioral Impairment Checklist (MBI-C), and explore its factor structure when employed as a self-report and informant rated tool.

Design: Population based cohort study.

Setting: Online testing via the PROTECT study (http://www.protectstudy.org.uk)

Participants: 5,742 participant-informant dyads.

Measurements: Both participants and informants completed the MBI-C. The factor structure of the MBI-C was evaluated by exploratory factor analysis (EFA).

Results: The most common MBI-C items as rated by self-report and informants related to affective dysregulation (mood/anxiety symptoms), being present in 34% and 38% of the sample respectively. The least common were items relating to abnormal thoughts and perception (psychotic symptoms) (present in 3 and 6% of the sample respectively). There were only weak correlations between self-report and informant-report MBI-C responses. EFA for both sets of respondent answers indicated a five-factor solution for the MBI-C was appropriate, reflecting the hypothesized structure of the MBI-C.

Conclusion: This is the largest and most detailed report on the frequency of MBI symptoms in a non-dementia sample. The full spectrum of MBI symptoms was present in our sample, whether rated by self-report or informant report. However, we show that the MBI-C performs differently in self-report versus informant-report situations, which may have important implications for the use of the questionnaire in clinic and research.

Keywords: MBI-C, Mild Behavioral Impairment, Dementia, SCD

Introduction

Neuropsychiatric symptoms (NPS) are common in dementia and Mild Cognitive Impairment (MCI) (Mortby *et al.*, 2018c). It is well established that NPS are associated with a significantly worse clinical disease course (Paulsen *et al.*, 2000; Wergeland *et al.*, 2015) and, in the case of MCI, a higher likelihood of presentation to clinical care (Cieslak *et al.*, 2018; Ismail *et al.*, 2017b) and of progression to dementia (David *et al.*, 2016; Forrester *et al.*, 2016; Peters *et al.*, 2013; Pink *et al.*, 2015; Rosenberg *et al.*, 2013; Taragano *et al.*, 2018; Taragano *et al.*, 2009; Wergeland *et al.*, 2015). This latter point has led to an increasingly intense interest in the question of whether NPS emergent before dementia may represent a marker for the very earliest stages of disease, a key priority for clinical trial recruitment and other early dementia intervention strategies (Mortby *et al.*, 2018a).

Mild Behavioral Impairment (MBI) is a neurobehavioral syndrome, which describes a spectrum of later life emergent, sustained, but sometimes subtle NPS. MBI centers around changes in behavior or personality in the domains of decreased interest, drive and motivation (apathy) (Sherman *et al.*, 2018), affective/emotional dysregulation (mood and anxiety symptoms) (Ismail *et al.*, 2018a), impulse dyscontrol (agitation, aggression, abnormal reward salience), social inappropriateness (impaired social cognition) (Desmarais *et al.*, 2018) and abnormal thoughts and perception (psychotic symptoms i.e. delusions and hallucinations) (Fischer and Agüera-Ortiz, 2018). Provisional diagnostic criteria have been developed which mandate that at least one symptom be present, at least intermittently for ≥6 months which is sufficient to cause at least minimal impairment in relationships, social functioning or work (Ismail *et al.*, 2016b). MBI must not form part of a dementia syndrome or be attributable to another psychiatric condition, as it is a pre-dementia syndrome.

After the development of the MBI syndrome, it became apparent that there were few ways of accurately measuring or detecting MBI. Rating scales traditionally used to assess neuropsychiatric symptoms include the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994), Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield and Billig, 1986) and Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) (Reisberg *et al.*, 1987), all of which were developed for dementia populations as opposed to preclinical/prodromal populations, and all of which have substantially shorter reference times than the 6 months required for MBI. Studies have used the NPI to estimate MBI prevalence by mapping NPI items onto MBI domains. The drawback of this approach is the relatively short reference range of the NPI of 1 month, which increases the possibility of false positives and, accordingly, overestimate the prevalence of MBI. In a community population-based study, MBI prevalence was 43.1% in subjective cognitive decline (SCD), and 48.9% in mild cognitive impairment (Mortby *et al.*, 2018b). In a cognitive neurology clinic population, the prevalence was higher still at 76.5% in SCD, and 85.3% in MCI (Sheikh *et al.*, 2018). If MBI is to detect those who are at high risk of incident cognitive decline and dementia for further assessment, workup or biomarker sampling, there is limited utility with these high frequencies. Thus, the MBI-C was designed through an iterative Delphi consensus including clinical and research experts in preclinical and prodromal dementia. Developed explicitly as a case ascertainment instrument for MBI, the MBI-C, is a 34 item questionnaire designed to be completed by patients, informants or clinicians, providing information on symptoms and behaviors as they are described in the MBI criteria. The MBI-C represents a potential advancement over existing tools because it captures explicitly MBI symptoms as they present in functionally independent community dwelling older adults, in contrast to those NPS that are more specific to dementia (e.g. resisting care, rummaging, importuning), and has a reference period of 6 months rather than 2-4 weeks as is the case with most other scales (Ismail *et al.*, 2017a). A limited amount of validation work has been carried out on the MBI-C thus far. Using the MBI-C in a primary care population, MBI prevalence was determined to be 5.8% in SCD (Mallo *et al.*, 2018b), and 14.2% in MCI (Mallo *et al.*, 2018a), with cut points of 8.5 and 6.5 respectively demonstrating

acceptable sensitivity and specificity for clinically diagnosed MBI according to the ISTAART diagnostic criteria (Mallo *et al.*, 2018b). Subsequent work has shown that the 8.5 cut point is also associated with subtle cognitive decline in healthy older adults (Creese *et al.*, 2019). Further, the MBI-C has demonstrated internal consistency, test-retest reliability (Mallo *et al.*, 2018c), and discriminative validity from the NPI (Kang *et al.*, 2018; Mallo *et al.*, 2018c). In terms of imaging and biomarker validations, the MBI-C is associated with worsening cognition and temporal lobe atrophy in those with Parkinson's Disease (Monchi *et al.*, 2018). Very recent data has correlated MBI-C score with PET ß-amyloid burden, *in those with normal cognition*, again supporting the utility of the MBI-C in case finding for early stage neurodegenerative disease in advance of overt cognitive impairment (Lussier *et al.*, 2019). However, it is not yet known whether there are differences in risk of cognitive decline associated with scores aggregated by MBI domain, as these longitudinal data are yet to emerge. As research into MBI grows, a better understanding of the psychometric properties of the MBI-C is required in order to inform the appropriate clustering of symptoms in future clinical studies. To our knowledge no such work has been published in this area.

There is clearly an imperative to gain a more detailed understanding about the presentation of MBI in the cognitively normal community population in order to fully understand associated risk of incident cognitive decline and dementia. Understanding the properties of the MBI-C is a logical starting point but surprisingly little is known about even the most basic questions of prevalence and the distribution of individual symptoms when assessed by the scale. The only study to address this question used the NPI as a proxy for MBI (by roughly mapping NPI items onto the five MBI domains) and found 3, 17, 16, 5 and 1% prevalence of apathy, mood/anxiety, impulse dyscontrol, social inappropriateness and psychosis respectively in cognitively normal individuals (Mortby *et al.*, 2018b). A similar study but in a neurology clinic sample with subjective cognitive impairment (SCI), used a transformation of NPI-Q (a shorter version of the NPI) scores and reported significantly higher frequencies, likely to be in part a result of

participants being sampled from a clinic rather than the general population in addition to the inherent limitations (described above) in using the NPI to rate MBI in non-dementia samples (Sheikh *et al.*, 2018). Another major limitation is that the NPI is based on carer interview, which may not be appropriate for cognitively normal populations. The MBI-C has been designed for both patient and proxy informant ratings but it is not known whether there are differences according to respondent, an important question when rating symptoms in the cognitively normal population as these patients tend to attend clinic without informants.

In this study we undertook an examination of the prevalence of MBI as measured by the MBI-C in a large cohort of participant-informant dyads and explored its latent structure with Exploratory Factor Analysis (EFA). The size of the cohort allowed us to undertake analysis at the single symptom level, providing the most detailed profiling of the prevalence of MBI and the properties of the MBI-C to date.

Methods

Participants

Participants were drawn from the Platform for Research Online to Investigate Genetics and Cognition in Aging (PROTECT) website (www.protect-exeter.org.uk). PROTECT is a UK-based 25-year longitudinal online research study which gathers longitudinal data to examine the impact of lifestyle, medical and genetic risk factors of cognitive health and dementia in older adults. Twenty-five thousand people are currently enrolled on PROTECT but this study focuses on a subset who of 5,742 participant-informant dyads who had completed the MBI-C at the time of the data freeze for this analysis. Inclusion criteria for both participants and

informants were: 1) age 50 or over; 2) regular access to a computer and the internet; and 3) no diagnosis of dementia. Informants were required to have known the participant for at least 10 years. Participants with a self-reported history of psychotic or neurodevelopmental disorder (n=34, ascertained by asking participants to self-report a diagnosis), major depression (n=688, ascertained by a PHQ-9 score >14), MCI (n=22, asking participants to self-report a diagnosis), stroke (n=109, self-report) or Parkinson's disease (n=16, self-report) were excluded to remove confounding of the MBI ratings in accordance with the ISTAART-AA MBI criteria (Ismail *et al.*, 2016a). This resulted in the exclusion of 836 people (there was some overlap in participants with these conditions). Informed consent was given through an electronic online process and ethical approval was gained through the London Bridge National Research Ethics Committee (Reference: 13/LO/1578). Participants were prospectively recruited from November 2015 through both local and national publicity. Invitations were also sent to persons registered for existing research studies at the Institute of Psychiatry, Psychology and Neuroscience at King's College London.

Procedure

Participants completed a range of online questionnaires, covering demographics (age, gender, educational level), mental health (to establish psychiatric or neurodevelopmental disorder), and the MBI-C. The MBI-C was completed by both participants and their informants at the same time point.

The Mild Behavioral Impairment Checklist (MBI-C)

The MBI-C comprises 34 questions covering neuropsychiatric domains relevant to preclinical and prodromal dementia (Ismail *et al.*, 2017a). Each item is rated on a scale of 0 to 3 based on severity. MBI scoring was examined at the single item level and the domain level (any symptom present vs no symptoms present). To be rated as present, symptoms must be present for at least six months (continuously, or intermittently) and must represent a change from a longstanding pattern of behavior. Each question is answered "Yes" or "No", and, if "Yes", the item is rated according to severity: 1 = mild (noticeable, but not a significant change); 2 = moderate (significant, but not a dramatic change); 3 = severe (very marked or prominent, a dramatic change).

Analysis

In this descriptive analysis of the MBI-C, frequency tables of symptom prevalence at the individual item level were produced for both participant and informant responses. We also grouped items according to their questionnaire domain creating a binary present (score of >0 on any domain item) vs. absent (score of 0 for all domain items) score for each.

Exploratory factor analysis (EFA, chosen because it is more suited to scale refinement in instances where the number of latent variables is driven by theory than other dimension reduction methods like principal components analysis) was carried out on self and informant MBI-C response data in R version 3.4.2 using the *psych* package. Parallel analysis was used to help determine the appropriate number of factors to extract. An oblique rotation (oblimin) was applied and the factor extraction method set to principal axis. This form of EFA is robust enough to moderate any deviation form normality within the data. As the development of the MBI-C was theory driven, we anticipated a particular factor structure would emerge reflecting the five domains of the questionnaire. To establish how many factors should be extracted, the

theory underpinning the MBI-C domain groupings as per the questionnaire was considered alongside parallel analysis of 1,000 data sets using a 95% cutoff (O'Connor, 2000). A factor loading cut-off of 0.4 used was for interpretation of a reasonable item loading on a factor (Velicer *et al.*, 1982). Cross loading items were defined as those with a less than 0.2 difference between loadings on single items on different factors.

Results

Descriptive analyses

5,742 participant-informant dyads were available for analysis (twenty cases with missing data were excluded). The average age of participants was 62 (SD 6.91; range 50-88) and 73% were female. Fifty-seven percent of participants were educated to undergraduate degree level of higher.

The median non-zero total MBI-C score on the informant-report scale was slightly higher (4; maximum score 53; interquartile range 6) than the self-report scale (3, maximum score 57; interquartile range 4) and 2,577 (45%) people were rated as having any MBI-C symptom present (i.e. MBI-C total>0) according to self-report and 2,938 (54%) according to informant report. Both participants and informants rated emotional dysregulation as the most common MBI-C domain followed by impulse dyscontrol, decreased interest/motivation, social inappropriateness, and abnormal thoughts and perception. The frequency of any symptom in each domain was as follows (self-report %; informant-report %): decreased interest/motivation (17%; 24%); emotional dysregulation (34%; 38%); impulse dyscontrol (24%; 38%), social inappropriateness (4%; 12%) and abnormal thoughts and perception (3%; 6%). In general, for each of the 34 items the proportions of people reporting severe symptoms (rated 3) was a fraction of 1%. There were marginally more reports (no more than 3%) of moderate symptoms (rated 2), leaving the vast majority rating symptoms as 1 if they were present at all.

An item-level breakdown of prevalence of MBI as rated by the MBI-C is presented in Table 1. The most common single MBI-C items were contained within domains 2 (emotional dysregulation) and 3 (impulse dyscontrol) according to both self and informant ratings. Specifically, question 2.1 ‘Has the person developed sadness or appear to be in low spirits? Does she/she have episodes of tearfulness?’ was the most commonly rated symptom by both participants and informants, present at any severity in 21% and 23% of cases respectively. The least common symptoms were those relating to hallucinations, present in less than 1% of the sample.

Table 1 Prevalence of the 34 MBI-C items rated by participants and their informants (N=5,742)

		MBI-C Severity Score (self-report)									MBI-C Severity Score (informant-report)								
MBI Item		**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot>0**	**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot>0**
Interest, motivation and drive																			
Q1.1	Has the person lost interest in friends, family, or home activities?	**5413**	94	**306**	5	**22**	0	**1**	0	329	**5292**	92	**392**	7	**52**	1	**6**	0	450
Q1.2	Does the person lack curiosity in topics that would usually have attracted her/his interest?	**5497**	96	**227**	4	**15**	0	**3**	0	245	**5412**	94	**304**	5	**25**	0	**1**	0	330
Q1.3	Has the person become less spontaneous and active – for example, is she/he less likely to initiate or maintain conversation?	**5380**	94	**342**	6	**18**	0	**2**	0	362	**5180**	90	**504**	9	**49**	1	**9**	0	562
Q1.4	Has the person lost motivation to act on her/his obligations or interests?	**5136**	89	**583**	10	**21**	0	**2**	0	606	**5030**	88	**660**	11	**48**	1	**4**	0	712
Q1.5	Is the person less affectionate and/or lacking in emotions when compared to her/his usual self?	**5422**	94	**296**	5	**21**	0	**3**	0	320	**5095**	89	**556**	10	**83**	1	**8**	0	647
Q1.6	Does she/he no longer care about anything?	**5545**	97	**188**	3	**8**	0	**1**	0	197	**5530**	96	**192**	3	**18**	0	**2**	0	212
	TOTAL FOR DOMAIN	**4749**								**993**	**4359**								**1383**
Mood or anxiety symptoms																			
Q2.1	Has the person developed sadness or appear to be in low spirits? Does she/she have episodes of tearfulness?	**4525**	79	**1092**	19	**115**	2	**10**	0	1217	**4447**	77	**1097**	19	**170**	3	**28**	0	1295
Q2.2	Has the person become less able to experience pleasure?	**5160**	90	**541**	9	**36**	1	**5**	0	582	**4993**	87	**657**	11	**83**	1	**9**	0	749
Q2.3	Has the person become discouraged about their future or feel that she/he is a failure?	**4812**	84	**856**	15	**64**	1	**10**	0	930	**4766**	83	**830**	14	**127**	2	**19**	0	976

MBI Item		MBI-C Severity Score (self-report)									MBI-C Severity Score (informant-report)								
		0	%	1	%	2	%	3	%	Tot> 0	0	%	1	%	2	%	3	%	Tot >0
Q2.4	Does the person view herself/himself as a burden to family?	**5582**	97	**141**	2	**17**	0	**2**	0	160	**5486**	96	**221**	4	**27**	0	**8**	0	256
Q2.5	Has the person become more anxious or worried about things that are routine (e.g. events, visits, etc.)?	**4929**	86	**752**	13	**55**	1	**6**	0	813	**4646**	81	**954**	17	**125**	2	**17**	0	1096
Q2.6	Does the person feel very tense, having developed an inability to relax, or shakiness, or symptoms of panic?	**5318**	93	**384**	7	**34**	1	**6**	0	424	**5170**	90	**491**	9	**63**	1	**18**	0	572
	TOTAL FOR DOMAIN	**3771**								**1971**	**3532**								**2210**
Ability to delay gratification and control behavior, impulses, oral intake and/or changes in reward																			
Q3.1	Has the person become agitated, aggressive, irritable, or temperamental?	**5012**	87	**693**	12	**37**	1	**0**	0	730	**4493**	78	**1096**	19	**138**	2	**15**	0	1249
Q3.2	Has she/he become unreasonably or uncharacteristically argumentative?	**5447**	95	**283**	5	**12**	0	**0**	0	295	**4904**	85	**729**	13	**97**	2	**12**	0	838
Q3.3	Has the person become more impulsive, seeming to act without considering things?	**5614**	98	**122**	2	**6**	0	**0**	0	128	**5370**	94	**331**	6	**38**	1	**3**	0	372
Q3.4	Does the person display sexually disinhibited or intrusive behaviour, such as touching (themselves/others), hugging, groping, etc., in a manner that is out of character or may cause offence?	**5725**	100	**14**	0	**2**	0	**1**	0	17	**5694**	99	**42**	1	**6**	0	**0**	0	48

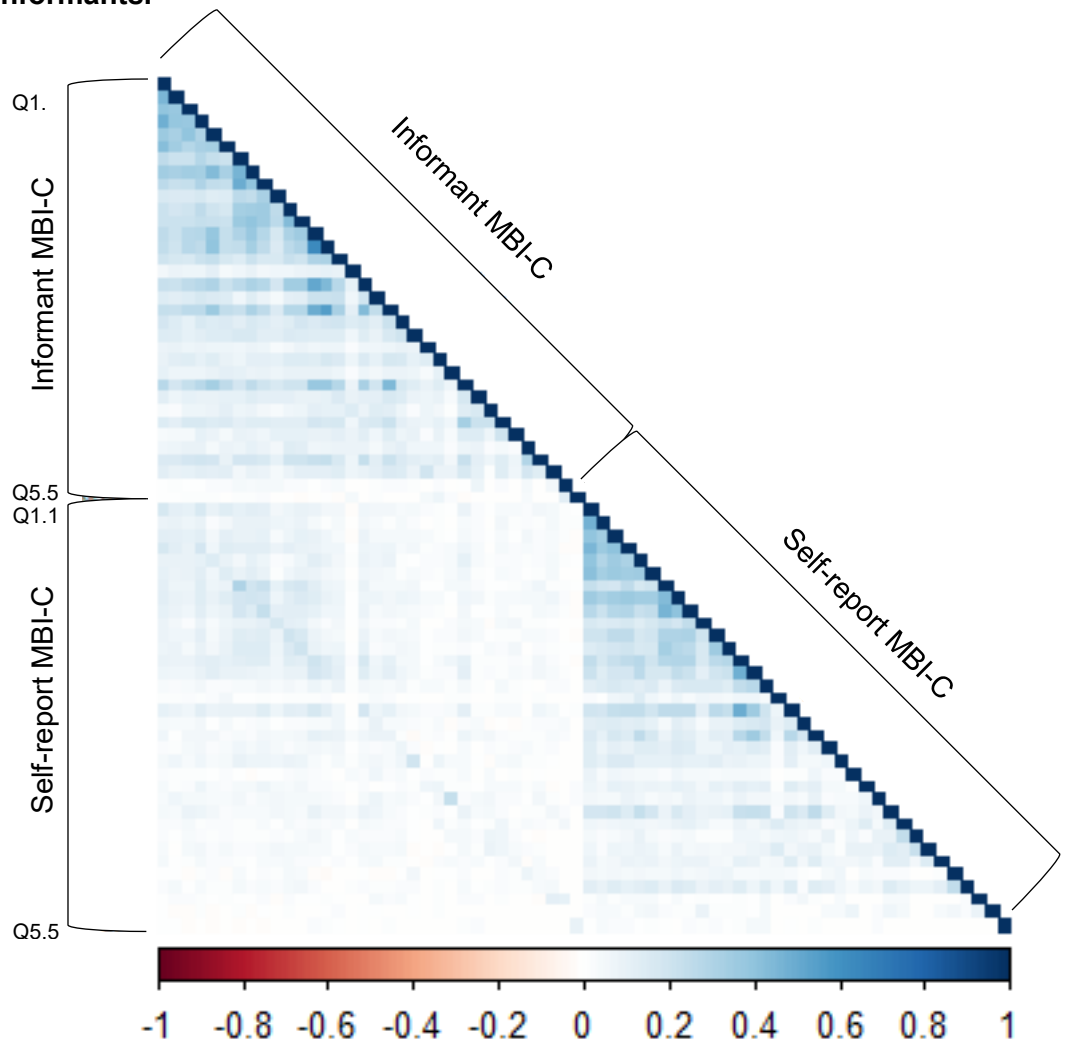
		MBI-C Severity Score (self-report)									MBI-C Severity Score (informant-report)								
MBI Item		**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot>0**	**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot>0**
Q3.5	Has the person become more easily frustrated or impatient? Does she/he have troubles coping with delays, or waiting for events or for their turn?	**5052**	88	**657**	11	**31**	1	**2**	0	690	**4613**	80	**1009**	18	**103**	2	**17**	0	1129
Q3.6	Does the person display a new recklessness or lack of judgement when driving (e.g. speeding, erratic swerving, abrupt lane changes, etc.)?	**5655**	98	**85**	1	**1**	0	**1**	0	87	**5463**	95	**251**	4	**25**	0	**3**	0	279
Q3.7	Has the person become more stubborn or rigid, i.e., uncharacteristically insistent on having their way, or unwilling/unable to see/hear other views?	**5584**	97	**152**	3	**5**	0	**1**	0	158	**4912**	86	**729**	13	**88**	2	**13**	0	830
Q3.8	Is there a change in eating behaviors (e.g., overeating, cramming the mouth, insistent on eating only specific foods, or eating the food in exactly the same order)?	**5676**	99	**59**	1	**6**	0	**1**	0	66	**5591**	97	**124**	2	**19**	0	**8**	0	151
Q3.9	Does the person no longer find food tasteful or enjoyable? Are they eating less?	**5553**	97	**180**	3	**7**	0	**2**	0	189	**5480**	95	**237**	4	**19**	0	**6**	0	262
Q3.10	Does the person hoard objects when she/he did not do so before?	**5725**	100	**17**	0	**0**	0	**0**	0	17	**5686**	99	**49**	1	**5**	0	**2**	0	56
Q3.11	Has the person developed simple repetitive behaviors or compulsions?	**5644**	98	**95**	2	**3**	0	**0**	0	98	**5589**	97	**137**	2	**14**	0	**2**	0	153

MBI Item		MBI-C Severity Score (self-report)									MBI-C Severity Score (informant-report)								
		0	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot> 0**	**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot >0**
Q3.12	Has the person recently developed trouble regulating smoking, alcohol, drug intake or gambling, or started shoplifting?	**5618**	98	**106**	2	**17**	0	**1**	0	124	**5617**	98	**103**	2	**18**	0	**4**	0	125
	TOTAL FOR DOMAIN	**4383**								**1359**	**3584**								**2158**
Following societal norms and having social graces, tact, and empathy																			
Q4.1	Has the person become less concerned about how her/his words or actions affect others? Has she/he become insensitive to others' feelings?	**5582**	97	**156**	3	**4**	0	**0**	0	160	**5184**	90	**501**	9	**52**	1	**5**	0	558
Q4.2	Has the person started talking openly about very personal or private matters not usually discussed in public?	**5701**	99	**38**	1	**3**	0	**0**	0	41	**5654**	98	**78**	1	**10**	0	**0**	0	88
Q4.3	Does the person say rude or crude things or make lewd sexual remarks that she/he would not have said before?	**5728**	100	**14**	0	**0**	0	**0**	0	14	**5695**	99	**45**	1	**1**	0	**1**	0	47
Q4.4	Does the person seem to lack the social judgement she/he previously had about what to say or how to behave in public or private?	**5719**	100	**22**	0	**1**	0	**0**	0	23	**5603**	98	**131**	2	**8**	0	**0**	0	139
Q4.5	Does the person now talk to strangers as if familiar, or intrude on their activities?	**5673**	99	**67**	1	**2**	0	**0**	0	69	**5640**	98	**96**	2	**6**	0	**0**	0	102
	TOTAL FOR DOMAIN	**5488**								**254**	**5045**								**697**
Strongly held beliefs and sensory experiences																			

		MBI-C Severity Score (self-report)									MBI-C Severity Score (informant-report)								
MBI Item		**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot> 0**	**0**	**%**	**1**	**%**	**2**	**%**	**3**	**%**	**Tot >0**
Q5.1	Has the person developed beliefs that they are in danger, or that others are planning to harm them or steal their belongings?	**5718**	100	**23**	1	**1**	0	**0**	0	24	**5683**	99	**51**	1	**7**	0	**1**	0	59
Q5.2	Has the person developed suspiciousness about the intentions or motives of other people?	**5632**	98	**104**	3	**5**	0	**1**	0	110	**5476**	95	**250**	4	**15**	0	**1**	0	266
Q5.3	Does she/he have unrealistic beliefs about her/his power, wealth or skills?	**5729**	100	**11**	0	**0**	0	**2**	0	13	**5696**	99	**39**	1	**7**	0	**0**	0	46
Q5.4	Does the person describe hearing voices or does she/he talk to imaginary people or “spirits”?	**5731**	100	**10**	0	**1**	0	**0**	0	11	**5735**	100	**6**	0	**1**	0	**0**	0	7
Q5.5	Does the person report or complain about, or act as if seeing things (e.g. people, animals or insects) that are not there, i.e., that are imaginary to others?	**5731**	100	**11**	0	**0**	0	**0**	0	11	**5733**	100	**9**	0	**0**	0	**0**	0	9
	TOTAL FOR DOMAIN	**5589**								**153**	**5415**								**327**

Informant-report frequencies were higher than self-report frequencies for 32 out of 34 MBI-C items (Table1). The two items where self-report frequencies were higher were those relating to auditory and visual hallucinations (questions 5.4 and 5.5). The impulse dyscontrol, social inappropriateness and abnormal thoughts and perception domains contained the highest levels of discordance in frequency ratings of participants and informants. In particular, the frequency of social inappropriateness and abnormal thoughts and perception symptoms reported by participants as a whole was less than half of that reported by informants. Frequencies of questions 3.2, 3.3, 3.4, 3.6, 3.7 and 3.10 reported by participants were one third the frequency reported by informants (Table 1). Self-reported frequencies for decreased interest/motivation and emotional dysregulation, while lower, were more comparable to informant-reported frequencies. Figure 1 shows a correlation plot of every MBI-C item rated by participants and informants. The lower left quarter of the plot represents the correlations between MBI-C items rated by participants and informants. Overall correlations between the same items rated by participants and informants did not exceed 0.3, indicating a high level of disagreement in responses, but some structure was evident within self-report and informant-report responses.

Figure 1 Spearman correlation matrix of MBI-C items rated by participants and informants.



Exploratory Factor Analysis of the MBI-C

We next conducted EFA on self-report and informant MBI-C responses. For both self-report and informant responses Bartlett's test of sphericity (33,507.16, df: 561; $p<0.001$; 49,573.36; df: 561; $p<0.001$ respectively) and the Kaiser-Meyer-Olkin Measure of Sampling Adequacy (0.9 and 0.92 respectively) indicated that MBI-C items were sufficiently related to perform factor analysis.

Self-report MBI-C

The decision of how many factors to extract was driven by a priori theory underpinning the development of the MBI-C, and the inspection of the scree plot produced by parallel analysis. Parallel analysis indicated a solution of between 4 and 11 factors. The factors from simulated data have lower Eigen values than the actual data up to factor 7 and between factor 8 and 11 the values were the same. The MBI-C has 34 items, so an 11-factor solution was not deemed useful (supplementary figure 1). As the MBI-C was developed on a theoretical basis to reflect 5 symptom domains, we elected to extract 5 factors from the analysis. A 6-factor solution was statistically similar but led to questions 5.1 and 5.2 not loading onto any factors. The resulting output is shown in Table 2. The overall model fit was acceptable (Tucker Lewis Index=0.902; RMSEA= 0.032, 90%CI 0.031-0.033; RMSR=0.02). Factor correlations are shown in the supplementary material.

The five factors covered 19 (56%) of the 34 items. Thus, not all MBI-C items loaded onto factors, however, in the main those that did loaded exclusively onto one factor.

All MBI-C interest/motivation/drive (1.1-1.6) questions loaded onto the first factor, termed ‘apathy’. The second factor was ‘affect’, with loadings from all but one of the affective

regulation items, the sole item not loading related to feeling a burden to family (2.4). We termed the third factor 'agitation' to reflect the four items (3.1, 3.2, 3.5, 3.7) from the impulse dyscontrol domain which loaded onto it; items not loading from this domain related to sexual disinhibition, compulsive behaviors and recklessness. Items 4.2, 4.3 and 4.4 of the social inappropriateness domain loaded onto the 'disinhibition' factor and finally the two items relating to simple delusions (5.1 and 5.2) loaded onto the fifth factor, termed 'suspiciousness' to reflect the low loadings of the hallucinations and grandiose delusion items. There was minimal cross loading; question 2.2 (ability to experience pleasure) had moderate loading onto factor 1 (0.36) but a higher loading on factor 2 (0.41).

Table 2 Factor loadings from exploratory factor analysis of MBI-C self-report

	Factor					
MBI-C Item	**Apathy**	**Affect**	**Agitation /irritability**	**Disinhibition**	**Suspicion**	**Communality**
Q1.1	**0.73**	-0.01	-0.03	0.02	-0.01	0.52
Q1.2	**0.66**	0	-0.01	-0.07	-0.02	0.41
Q1.3	**0.6**	0.03	0.01	0.02	0.04	0.41
Q1.4	**0.59**	0.12	-0.01	0.04	-0.04	0.42
Q1.5	**0.51**	-0.06	0.19	0.03	0.01	0.37
Q1.6	**0.59**	0.02	0.01	0	0.06	0.39
Q2.1	0.01	**0.69**	0.02	0.02	0	0.49
Q2.2	0.36	**0.41**	0.02	0.05	0.03	0.48
Q2.3	0.15	**0.53**	0.03	0.06	0.05	0.45
Q2.4	0.11	0.25	0.01	0.06	0.16	0.18
Q2.5	0.05	**0.45**	0.14	-0.02	0.09	0.33
Q2.6	-0.02	**0.46**	0.18	-0.04	0.08	0.32
Q3.1	-0.04	0.17	**0.67**	0	-0.03	0.53
Q3.2	0.02	-0.02	**0.69**	-0.01	-0.03	0.47
Q3.3	0.07	-0.06	0.35	0.05	0.15	0.21
Q3.4	-0.02	0.03	0.05	0.19	-0.01	0.04
Q3.5	0.01	0.13	**0.54**	0.03	0.03	0.39
Q3.6	0.17	-0.11	0.25	0.05	0.02	0.12
Q3.7	0.11	-0.19	**0.48**	0.04	0.1	0.29
Q3.8	0.09	0.03	0.11	0.04	0.12	0.08
Q3.9	0.13	0.07	-0.01	0.03	0.07	0.05
Q3.10	0.04	0.01	-0.01	0.19	-0.02	0.04
Q3.11	0	0.03	0.14	0.13	0.05	0.06
Q3.12	-0.02	0.03	0.05	0.13	0.04	0.03

Q4.1	0.17	-0.16	0.29	0.18	0.11	0.23
Q4.2	-0.06	0.05	-0.03	**0.5**	0.03	0.24
Q4.3	-0.03	0	-0.03	**0.44**	-0.05	0.18
Q4.4	0.01	-0.02	0	**0.46**	-0.03	0.20
Q4.5	-0.01	-0.01	0.06	0.3	0.07	0.12
Q5.1	-0.02	0.02	-0.07	-0.1	**0.48**	0.21
Q5.2	-0.02	0.03	-0.01	0.05	**0.6**	0.38
Q5.3	0.03	-0.03	0.01	0	0.01	0.00
Q5.4	0.02	0	-0.03	0.03	0.08	0.01
Q5.5	0.03	0.01	0.03	-0.03	-0.02	0.00

Informant-report MBI-C

The decision on how many factors to extract from the informant-report data followed the same process as described above for the self-report data; i.e. a 5-factor model was found to be the best solution, with good model fit statistics (Tucker Lewis Index=0.909; RMSEA= 0.037 90%CI 0.036-0.038; RMSR=0.02). Factor correlations are shown in the supplementary material.

The informant rated MBI-C displayed a similar factor structure to the self-report MBI-C, so the factor naming was kept the same, with the exception of factor 5. Twenty items (59%) loaded above 0.4 (Table 3). All items from interest motivation and drive and affective regulation loaded onto a single factor each (the apathy and affect factors). Items 3.1, 3.2, 3.5, 3.7 from the impulse control domain loaded onto the agitation factor; items not loading from this domain related to sexual disinhibition, compulsive behaviors and recklessness. Items 4.2 and 4.4 were the only items to load onto the disinhibition factor although item 4.3 loaded at 0.39. The modest cross loading of item 2.2 (loading onto motivation/interest and affect somewhat) was present but to a lesser extent than in the self-report MBI-C. Factor 5 was the only factor whose name it was appropriate to change from the self-report MBI-C EFA. All the items covering delusions (items 5.1, 5.2 and 5.3, reflecting suspiciousness and more grandiose type delusions) but

none of the hallucination items loaded onto this factor. Because of this we labeled this factor 'delusions' in the informant rated MBI-C.

Table 3 Factor loadings from exploratory factor analysis of MBI-C informant report

	Factor					
MBI-C Item	**Apathy**	**Affect**	**Agitation /irritability**	**Disinhibition**	**Delusions**	**Communality**
Q1.1	**0.73**	0.04	-0.04	0.02	0.02	0.56
Q1.2	**0.68**	0.03	-0.06	-0.01	0.02	0.45
Q1.3	**0.6**	0.01	0.09	-0.02	0	0.41
Q1.4	**0.55**	0.09	0.06	-0.01	0.03	0.41
Q1.5	**0.48**	-0.06	0.33	-0.02	-0.01	0.43
Q1.6	**0.58**	0.03	0.01	0.08	-0.01	0.40
Q2.1	0.05	**0.7**	-0.03	0.01	-0.04	0.50
Q2.2	0.26	**0.48**	0.1	0.01	-0.03	0.50
Q2.3	0.1	**0.68**	-0.04	-0.01	0	0.52
Q2.4	0.01	**0.5**	-0.08	0.1	-0.02	0.25
Q2.5	-0.05	**0.55**	0.13	0.01	0.11	0.41
Q2.6	-0.09	**0.59**	0.18	0.02	0.09	0.48
Q3.1	0.01	0.09	**0.78**	-0.04	-0.02	0.66
Q3.2	0.02	-0.02	**0.82**	-0.01	0	0.67
Q3.3	0.03	0.03	0.33	0.26	0.03	0.29
Q3.4	0.02	0	0.04	0.15	0.08	0.05
Q3.5	-0.02	0.16	**0.58**	0.04	0.03	0.48
Q3.6	0.03	-0.04	0.2	0.33	-0.01	0.20
Q3.7	0.06	-0.03	**0.63**	0.14	0.06	0.54
Q3.8	0.08	0.05	0.05	0.3	0.16	0.21
Q3.9	0.05	0.13	0.01	0.23	0.09	0.14
Q3.10	0.06	-0.02	-0.06	0.29	0.16	0.13
Q3.11	-0.01	0.04	0.11	0.19	0.09	0.10
Q3.12	0.09	0.07	0.04	0.04	0.01	0.04
Q4.1	0.13	-0.05	0.4	0.25	0.07	0.40
Q4.2	-0.01	0.09	-0.05	**0.41**	0.09	0.21
Q4.3	-0.06	0.06	0.02	0.39	-0.09	0.15
Q4.4	0.04	0.03	0.04	**0.5**	-0.06	0.28
Q4.5	-0.09	0.09	0.02	0.28	0.01	0.09
Q5.1	0	0.01	-0.04	-0.05	**0.71**	0.48
Q5.2	0.01	0.07	0.18	0	**0.41**	0.27
Q5.3	0.11	-0.05	-0.03	0.2	**0.41**	0.28
Q5.4	0.05	0.01	-0.05	0.12	0.01	0.02
Q5.5	0.02	0	-0.03	0.02	0.03	0.00

Discussion

This analysis of 5,742 participant-informant dyads from the PROTECT study provides an unparalleled level of insight into the symptom profile of Mild Behavioral Impairment (MBI), as rated by the MBI-C, in a non-dementia non-MCI sample. These symptoms represent new data on the profile of a known risk factor for dementia in a cognitively normal sample.

The ratings from both participants and informants show that the most common MBI symptoms in our sample are those relating to mood/anxiety (34 and 38% respectively) while the least common are those relating to psychotic symptoms (3 and 6% respectively). These frequencies are considerably higher than those reported by Mortby et al. (2018b) in their cognitively normal population, with the difference being particularly pronounced for the decreased motivation domain. Mortby et al. used the NPI to rate MBI symptoms and these differences may be explained by the fact decreased motivation is underrepresented on the NPI or that the reference range of the NPI is 4 weeks (compared to six months on the MBI-C). In the MBI-C, apathy is more syndromically captured with questions on interest, initiative, and emotional reactivity, broadening the spectrum of changes captured by the scale. It is also possible that our sample contains some individuals with undiagnosed or very early MCI, where neuropsychiatric symptoms will be more common. Individuals in the Mortby et al. study underwent clinical screening for cognitively normal status, which would result in a sample with a much lower frequency of symptoms.

We can conclude that our findings clearly show that informant- and self-report versions of the MBI-C perform differently, and do not capture the exactly same groups, which has important implications for study design in the cognitively normal population. The practical implications of this finding are that self- and informant-report versions of the MBI-C are not interchangeable,

but may provide complementary information. It is not clear from this study what the reasons for the differences between groups may be. It is possible that some of it is attributable to error on the part of the informants or the relationship between the two (e.g. spouse, parent etc), the variability of observation periods or time spent with the participant, and the ability or inability to access the internal world of the participant if that internal world had not been overtly expressed (eg. admitting that one feels like a burden to the family, or that one has suspiciousness or hallucinations). However the informant was required to know the participant well and for at least 10 years, which increases confidence that their responses are based on sound experience, a fair knowledge of the participant and their baseline behavioral state, and the ability to observe changes from that baseline. Alternatively, some of the differences may also be related to anosognosia or the loss of insight that the participant has into their symptoms. For example, anosognosia can prevent the participant from endorsing items around irritability, impulsivity, new onset substance abuse, or socially inappropriate behavior, and thus the informant would give a more accurate response because the questions relating to behaviors, objectively observed by the informant. Intuitively, this is consistent with our findings of lower self-reported frequencies of impulse dyscontrol and social inappropriateness. However, more work is needed in this area. Most of the items with the highest rates of discordance (questions 3.2, 3.3, 3.4, 3.6, 3.7, 3.10 and all of the social inappropriateness domain except 4.5) all concern negative aspects of a person's character. When responding for themselves participants may not attribute much significance to these sorts of changes, or informants may attribute too much. If insight was a major driver, one would not expect ratings of visual hallucinations to be higher among self-report than informant report. To truly address this question, analysis of the emergent cognitive decline and its correlation with ratings will be necessary alongside in person clinical work ups and observation over longer periods.

For the participant EFA, factor structure was simple and reflected the MBI-C theoretical domains. The impulse dyscontrol domain of the MBI-C contains the largest number of

questions (12) and there was a clear distinction along phenomenological lines in the loadings of those items relating to agitation and irritability (Q3.1, 3.2, 3.5 and 3.7), which loaded >0.4, and those relating to impulsivity, gratification and compulsiveness, which did not load strongly. The social inappropriateness and abnormal thoughts and perception domains were also split. The interpretation of the social inappropriateness items is less straightforward as all items clearly relate to social judgement. One could speculate that items 4.1 and 4.5 (which do not load onto any factor) are focused on the impact of one's actions on others and who it is appropriate to engage with in public (requiring insight on the part of the participant, but based on observation and a judgment call on the part of the informant), while items 4.2, 4.3 and 4.4 concern the content of what it said or done in public (again, requiring insight on behalf of the participant, but likely much more objectively reported and observed by the informant). It is also worth noting that question 4.1 is framed as two questions ("Has the person become less concerned about how her/his words or actions affect others? Has she/he become insensitive to others' feelings?"). This could be interpreted in different ways by participants (i.e. some may focus on the former which is about "less concern" rather than "insensitivity", and our finding of no strong loading for this item may be in part a result of this. The two abnormal thoughts and perception items clearly relate to simple delusions while the grandiose delusions covered in item 5.3 and hallucinations do not load on to any factor. While the phenomenological distinction is consistent with the factor loadings it should be noted that items 5.3, 5.4 and 5.5 and extremely low frequency items so it is unlikely that they would load strongly onto any factor.

The informant EFA also reflected the domain structure of the MBI-C, in broadly the same way as the self-report responses, such that the factor labels were mostly appropriate for both sets of responses. The important exception is that item 5.3 ('Does she/he have unrealistic beliefs about her/his power, wealth or skills?') loaded with the other delusion items, which are persecutory in nature. These similarities and difference in the factor structure are interesting

but full testing of the hypothesis that both sets of respondents yield the same factor structure must be undertaken with confirmatory factor analysis in independent populations before such conclusions can be drawn.

The only item to display any cross loading in both self-report and informant rated MBI-C was question 2.2 (“Has the person become less able to experience pleasure”). Although the absolute loadings of this item onto apathy and affect were weak and moderate respectively for both self-report and informant responses, the difference in loading onto the two factors was small (0.36 on apathy factor and 0.41 on the affect factor of the self-report MBI-C), warranting some discussion. This question is designed to capture anhedonia, and the cross loading observed could reflect different interpretation of this question among respondents because anhedonia is a symptom of depression as well as reflecting apathy, specifically emotional apathy. There is a growing recognition of the importance of the distinction between apathy and depression as markers of dementia (Ismail *et al.*, 2018a; Palmer *et al.*, 2010; Sherman *et al.*, 2018; van Dalen *et al.*, 2018), so it is interesting that there is some loading across both affective and motivation/drive items of the MBI-C. The suggestion here is that, at least in the cognitively normal population, some refinement to the wording of this particular question may be necessary to capture this distinction in the MBI-C. Alternatively, these data raise questions as to whether or not psychiatric constructs developed for a general population, often reflecting neurodevelopmental disorders, accurately represent the emergence of neuropsychiatric symptoms in older adults. For some of these older adults the emerging symptoms are the index manifestation of a neurodegenerative disease (Masters *et al.*, 2015; Taragano *et al.*, 2018) and the symptoms may reflect different etiopathologies from symptoms in traditional psychiatric constructs. In our study, anhedonia is an item that is part of the major depression construct as it has been traditionally described, which might reflect apathy more than depression in a pre-clinical dementia population. Similar to the finding that “feeling a burden to the family” (an item seen in major depression in older adults) does not map onto a factor,

anhedonia in this population may be better subsumed by apathy because the “depression” seen in this population may be different from “depression” as is commonly described in the young adult and general adult population. Further investigation with longitudinal data will be required to explore this interesting finding. The robust longitudinal data suggesting that later life emergence of depression may often be the index manifestation of dementia, sometimes misdiagnosed as major depression, support the need to disentangle “major depression” from the mood and anxiety symptoms in preclinical and prodromal dementia (Almeida *et al.*, 2017; Ismail *et al.*, 2018b; Singh-Manoux *et al.*, 2017; Tapiainen *et al.*, 2017). The major immediate implication of the EFA relates the splitting or reorganization of some of the MBI-C domains. MBI-C usage is becoming more common and research will inevitably progress to the role of each domain in dementia risk or cognitive aging. A logical starting point would be to work at the domain level as specified by the MBI-C by simply summing scores or using a binary present/absent coding. However, our findings suggest that analyzing factor scores rather than simple summing of items may be more appropriate.

The relatively large number of low loading MBI-C items suggests that in this sample of older adults without dementia there are some items which are not relevant. Based on this information alone a case could be made for removing all of the weak loading items to create a shortened questionnaire. However, the purpose of the MBI-C must not be ignored. The MBI-C is designed to capture the whole spectrum of NPS which may be risk factors for, or early manifestations of, dementia in both community and clinical samples. Capturing emergent symptoms, including low frequency ones, will be important both in the clinic and for prospective research studies where use of the MBI-C is likely to increase in the coming years. Therefore, to avoid losing sensitivity for those less common, but important, items we would not recommend dropping any items from the MBI-C based on this EFA. The results of the present study should now inform further development of the MBI-C in the following ways. Firstly, studies should be undertaken in independent samples to confirm that factor structure reported

here. These samples should be drawn from cognitively normal and a range of clinical populations to explore the stability of the factor structure across different levels of cognitive impairment. Then, if the structure is confirmed using CFA and the same items continue to load poorly, inclusion of some items may be reconsidered. In particular, it may be the case that an abridged version of the MBI-C based on the results presented here is suitable for large scale population screening in relatively unimpaired populations. Finally, longitudinal data will also guide item evolution, and enable evaluation of the relative prognostic utility of each item and each factor for different types of dementia and cognitive decline in older adults. We feel we are still at early stages of understanding the psychometric properties of the MBI-C. We do not believe making drastic changes in a scale at present is warranted.

With regard to limitations, it should be noted that among respondents there was an overrepresentation of women and people with a higher than average education when compared the UK population, accordingly the prevalence of MBI symptoms reported in this sample may not represent those of the general population. We also tested individuals who did not have dementia so we would caution against generalizing the findings from this sample to MCI or possibly also to the wider cognitively normal population.

In summary we have presented a detailed overview of the prevalence of 34 individual MBI symptoms in a large sample of cognitively normal people, finding that the entire spectrum of symptoms is present to a greater or lesser extent. This, alongside the ease and low cost of online data collection, demonstrates the utility of the MBI-C in large-scale population screening for identifying MBI groups. We have also found that despite symptom frequencies being broadly the same in self-report and informant report, these two forms of administering the MBI-C do not capture the same groups, this may have important implications for the use of the questionnaire in clinic and research.

CONFLICTS OF INTEREST

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DESCRIPTION OF AUTHORS' ROLES

BC: study design, analysis and drafting of article; AG: analysis and drafting of article; HB: data collection and drafting of article; AC: data collection and drafting of article; DA: data collection and drafting of article; CB: data collection drafting of article drafting; ZI: study design, drafting of article.

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REFERENCES

Almeida, O., Hankey, G., Yeap, B., Golledge, J. and Flicker, L. (2017). Depression as a modifiable factor to decrease the risk of dementia. *Translational psychiatry*, 7, e1117.

Cieslak, A., Smith, E. E., Lysack, J. and Ismail, Z. (2018). Case series of mild behavioral impairment: toward an understanding of the early stages of neurodegenerative diseases affecting behavior and cognition. *International Psychogeriatrics*, 30, 273-280.

Cohen-Mansfield, J. and Billig, N. (1986). Agitated behaviors in the elderly. I. A conceptual review. *J Am Geriatr Soc*, 34, 711-721.

Creese, B.*, et al.* (2019). Mild Behavioral Impairment as a Marker of Cognitive Decline in Cognitively Normal Older Adults. *The American Journal of Geriatric Psychiatry*.

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A. and Gornbein, J. (1994). The Neuropsychiatric Inventory. *Neurology*, 44, 2308.

David, N. D., Lin, F., Porsteinsson, A. P. and Alzheimer's Disease Neuroimaging, I. (2016). Trajectories of Neuropsychiatric Symptoms and Cognitive Decline in Mild Cognitive Impairment. *Am J Geriatr Psychiatry*, 24, 70-80.

Desmarais, P., Lanctôt, K. L., Masellis, M., Black, S. E. and Herrmann, N. (2018). Social inappropriateness in neurodegenerative disorders. *International Psychogeriatrics*, 30, 197-207.

Fischer, C. E. and Agüera-Ortiz, L. (2018). Psychosis and dementia: risk factor, prodrome, or cause? *International Psychogeriatrics*, 30, 209-219.

Forrester, S. N., Gallo, J. J., Smith, G. S. and Leoutsakos, J.-M. S. (2016). Patterns of Neuropsychiatric Symptoms in Mild Cognitive Impairment and Risk of Dementia. *The American Journal of Geriatric Psychiatry*, 24, 117-125.

Ismail, Z.*, et al.* (2017a). The Mild Behavioral Impairment Checklist (MBI-C): A rating scale for neuropsychiatric symptoms in pre-dementia populations. *Journal of Alzheimer's disease : JAD*, 56, 929-938.

Ismail, Z.*, et al.* (2017b). A Systematic Review and Meta-Analysis for the Prevalence of Depression in Mild Cognitive Impairment. *JAMA psychiatry*, 74, 58-67.

Ismail, Z.*, et al.* (2018a). Affective and emotional dysregulation as pre-dementia risk markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria. *Int Psychogeriatr*, 30, 185-196.

Ismail, Z.*, et al.* (2018b). Affective and emotional dysregulation as pre-dementia risk markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria. *International Psychogeriatrics*, 30, 185-196.

Ismail, Z.*, et al.* (2016a). Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment. *Alzheimers Dement*, 12, 195-202.

Ismail, Z.*, et al.* (2016b). Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment. *Alzheimer's & Dementia*, 12, 195-202.

Kang, Y.*, et al.* (2018). Mild Behavioral Impairment (MBI) in MCi, SCD, and Normal Elderly: A Pilot Study for Validation of the MBI Checklist (MBI-C). *Alzheimers Dement*, 14, 793.

Lussier, F.*, et al.* (2019). Mild behavioral impairment is associated with β-amyloid and tau in cognitively intact elderly individuals. Human Amyloid Imaging Miami, USA.

Mallo, S. C.*, et al.* (2018a). Assessing Mild Behavioral Impairment with the Mild Behavioral Impairment-Checklist in People with Mild Cognitive Impairment. *J Alzheimers Dis*, 66, 83-95.

Mallo, S. C.*, et al.* (2018b). Assessing mild behavioral impairment with the mild behavioral impairment checklist in people with subjective cognitive decline. *International Psychogeriatrics*, 1-9.

Mallo, S. C.*, et al.* (2018c). Mild Behavioral Impairment Checklist (MBI-C): A Preliminary Validation Study. *Alzheimers Dement*, 14.

Masters, M. C., Morris, J. C. and Roe, C. M. (2015). "Noncognitive" symptoms of early Alzheimer disease: a longitudinal analysis. *Neurology*, 84, 617-622.

Monchi, O.*, et al.* (2018). What Can the Mild Behavioral Impairment Checklist (MBI-C) Tell Us about Cognition and Behavior in Parkinson's Disease. *Alzheimers Dement*, 14.
Mortby, M. E.*, et al.* (2018a). Dementia clinical trial implications of mild behavioral impairment. *Int Psychogeriatr*, 30, 171-175.
Mortby, M. E., Ismail, Z. and Anstey, K. J. (2018b). Prevalence estimates of mild behavioral impairment in a population-based sample of pre-dementia states and cognitively healthy older adults. *International Psychogeriatrics*, 30, 221-232.
Mortby, M. E., Lyketsos, C. G., Geda, Y. E. and Ismail, Z. (2018c). Special Issue on mild behavioral impairment and non-cognitive prodromes to dementia. *Int Psychogeriatr*, 30, 167-169.
O'Connor, B. P. (2000). SPSS and SAS programs for determining the number of components using parallel analysis and velicer's MAP test. *Behav Res Methods Instrum Comput*, 32, 396-402.
Palmer, K.*, et al.* (2010). Neuropsychiatric predictors of progression from amnestic-mild cognitive impairment to Alzheimer's disease: the role of depression and apathy. *J Alzheimers Dis*, 20, 175-183.
Paulsen, J. S.*, et al.* (2000). Incidence of and risk factors for hallucinations and delusions in patients with probable AD. *Neurology*, 54, 1965-1971.
Peters, M. E.*, et al.* (2013). Neuropsychiatric Symptoms as Risk Factors for Progression From CIND to Dementia: The Cache County Study. *The American Journal of Geriatric Psychiatry*, 21, 1116-1124.
Pink, A.*, et al.* (2015). Neuropsychiatric symptoms, APOE ε4, and the risk of incident dementia. *A population-based study*, 84, 935-943.
Reisberg, B., Borenstein, J., Salob, S. P., Ferris, S. H., Franssen, E. and Georgotas, A. (1987). Behavioral symptoms in Alzheimer's disease: phenomenology and treatment. *J Clin Psychiatry*, 48 Suppl, 9-15.
Rosenberg, P. B., Mielke, M. M., Appleby, B. S., Oh, E. S., Geda, Y. E. and Lyketsos, C. G. (2013). The association of neuropsychiatric symptoms in MCI with incident dementia and Alzheimer disease. *Am J Geriatr Psychiatry*, 21, 685-695.
Sheikh, F.*, et al.* (2018). Prevalence of mild behavioral impairment in mild cognitive impairment and subjective cognitive decline, and its association with caregiver burden. *International Psychogeriatrics*, 30, 233-244.
Sherman, C., Liu, C. S., Herrmann, N. and Lanctôt, K. L. (2018). Prevalence, neurobiology, and treatments for apathy in prodromal dementia. *International Psychogeriatrics*, 30, 177-184.
Singh-Manoux, A.*, et al.* (2017). Trajectories of Depressive Symptoms Before Diagnosis of Dementia: A 28-Year Follow-up Study. *JAMA psychiatry*.
Tapiainen, V., Hartikainen, S., Taipale, H., Tiihonen, J. and Tolppanen, A.-M. (2017). Hospital-treated mental and behavioral disorders and risk of Alzheimer's disease: A nationwide nested case-control study. *European Psychiatry*, 43, 92-98.
Taragano, F. E.*, et al.* (2018). Risk of Conversion to Dementia in a Mild Behavioral Impairment Group Compared to a Psychiatric Group and to a Mild Cognitive Impairment Group. *J Alzheimers Dis*, 62, 227-238.
Taragano, F. E.*, et al.* (2009). Mild behavioral impairment and risk of dementia. *The Journal of clinical psychiatry*, 70, 584-592.
van Dalen, J., van Wanrooij, L. L., Moll van Charante, E. P., Brayne, C., van Gool, W. A. and Richard, E. (2018). Association of apathy with risk of incident dementia: A systematic review and meta-analysis. *JAMA Psychiatry*, 75, 1012-1021.
Velicer, W. F., Peacock, A. C. and Jackson, D. N. (1982). A Comparison Of Component And Factor Patterns: A Monte Carlo Approach. *Multivariate Behav Res*, 17, 371-388.
Wergeland, J. N., Selbæk, G., Bergh, S., Soederhamn, U. and Kirkevold, Ø. (2015). Predictors for Nursing Home Admission and Death among Community-Dwelling People 70 Years and Older Who Receive Domiciliary Care. *Dementia and Geriatric Cognitive Disorders Extra*, 5, 320-329.